REMARKS

Reconsideration and withdrawal of the rejections of the application respectfully requested in view of the remarks and enclosures herewith, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 8-9 are pending in this application.

Claims 8-9 have been amended. SEQ ID NOS:3, 4 and 5 correspond to the proteins ALZASp, ALZASp1 and ALZASp2 referred to in the specification with the erroneous identifiers SEQ ID NO: 2, 6 and 15 (see, e.g., paragraph 50 of the specification as published). No new matter has been added by this amendment.

The Examiner is thanked for withdrawing the previous objections and rejections of record.

It is submitted that the claims as originally presented were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims, as previously presented, were not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions were made simply for clarification and to round out the scope of protection to which Applicants are entitled.

II. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 112 ARE OVERCOME

Claims 8 and 9 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to comply with the written description requirement, in particular, the recitation of "fragments of human antibodies".

Although Applicants do not agree with the Examiner, in the interest of expediting prosecution, the recitation of "fragments of human antibodies" has been removed from claims 8 and 9, thereby obviating the rejection.

Claims 8 and 9 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to comply with the enablement requirement, in particular, the recitation of "a method of passive vaccination to prevent and stop initiation and progression, respectively of Alzheimer's disease and other associated diseases".

Although Applicants do not agree with the Examiner, in the interest of expediting prosecution, the recitation of "to prevent and stop initiation and progression" has been removed from claims 8 and 9, thereby obviating the rejection in part.

According to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988),

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. 'The key word is undue, not experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Citations omitted]. *Id.* at 1404.

Determining whether undue experimentation is required to practice a claimed invention turns on weighing many factors summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), for example: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

Thus, it is respectfully submitted that for a proper Section 112, first paragraph, lack of enablement analysis, an Office Action must show that the *Wands* factors are not met. Simply, it is respectfully asserted that the lack of enablement rejection fails to provide a fact based analysis using the *Wands* factors that supports the proposition the claimed invention require **undue** experimentation.

The Examiner is respectfully reminded that a specification need not contain any example of the invention, as the issue is whether the disclosure enables one skilled in the art to practice the invention without undue experimentation. *In re Borkowski*, 422 F.2d 904, 164 USPQ 642 (CCPA 1970). Simply, a determination that undue experimentation is necessary to practice the invention does not necessarily follow from a lack of examples in the specification. And, the Examiner is further respectfully reminded that an applicant need not describe all actual embodiments of a claimed invention.

The Office Action asserts that no actual therapeutic data is disclosed in the specification from human patients or from an art-accepted animal model for Alzheimer's disease or associated

diseases. The Office Action alleges that the expression data is correlative and that Applicants have not established a nexus between such data and a method of passive vaccination to prevent and stop initiation and progression of Alzheimer's disease or associated diseases.

Applicants respectfully disagree. The ALZAS proteins were identified based upon Applicants' realization that there must be other genes within the APP locus with association to the AD and DS, and that at least one of these genes must also have a β-amyloid related component. Therefore, Applicants used a procedure which they had successfully used to find alternative genes, which are putative causative factors of other "genetic diseases", to search for such genes which might segregate with Alzheimer's disease, within the locus encoding the entire APP gene on chromosome 21 and the regions that flank the gene (see, e.g., paragraph 55 of the specification as published).

Therefore, based upon the Applicants' disclosure, one of skill in the art would believe that ALZAS proteins are not mere markers but rather causative agents of Alzheimer's disease or associated diseases.

Applicants' discovery that these molecules: (i) were expressed in (100%) of brains, lymphocytes and blood obtained from humans with Alzheimer's disease, (ii) elicited an antibody response in humans before clinical symptoms of the disease was detected, (iii) were not detected in normal individuals (normal=individuals below 30 years and individuals above 60 with no history of a neurodegenerative disease), and (iv) appeared in humans in accordance with the known incidence of Alzheimer's disease or associated diseases in the population,(i.e., they were detected in 2 of 5 clinically normal people over the age of 65 who appeared suspect for of Alzheimer's disease or associated diseases). Such data strongly supported involvement of ALZAS molecules in the etiology of Alzheimer's disease (see, e.g., paragraph 72 of the specification as published).

The specification also discloses that affinity purification of ALZAS on columns of anti-ALZAS-sepharose columns of patients indicate that the ALZAS protein is bound to human immunoglobulin fragments in Alzheimer's disease patients. This indicates that ALZAS is modulated by the immune systems in Alzheimer's disease victims, and may be a target for complement derived destruction (see McGeer P. L. and McGeer, E. G. Ann NY Acad. Sci. 777:213-220 1996) (see, e.g., paragraph 83 of the specification as published).

Accordingly, based upon the Applicants' disclosure, one of skill in the art would believe that ALZAS proteins are causative agents of Alzheimer's disease or associated diseases, that ALZAS proteins are modulated by the immune system in patients with Alzheimer's disease and that administration of antibodies against ALZAS proteins would result in vaccinating a patient against such diseases.

Therefore, there is a failure to provide a factual showing that the present application is not enabled. Absent factual evidence corresponding to the *Wands* factors above, the Section 112 rejection is improper and must be withdrawn.

Claims 8 and 9 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to set forth the subject matter which Applicants regard as their invention, in particular, the recitation of SEQ ID NOS corresponding to nucleic acid molecules and not amino acid molecules.

Applicants also respectfully point out that the claims have been clarified to recite SEQ ID NOS:3, 4 and 5 which correspond to the proteins ALZASp, ALZASp1 and ALZASp2, thereby obviating the rejection.

Accordingly, reconsideration and withdrawal of the Section 112 rejections is respectfully requested.

Reconsideration and withdrawal of the claim rejections is respectfully requested.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, a further interview with the Examiner and SPE are respectfully requested; and, the Office Action is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks, amendments and Exhibits submitted herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,

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